

REMARKS

Claims 1, 2, 6, 7, 10-12, 14, and 16-23 are pending with claims 3-5, 8-9, 13, and 15 canceled, and claims 16-23 added.

Claims Objections

Applicants acknowledge that claims 3-5, 8, 9, 13 and 15 stand objected as being dependent upon a rejected base claim, but would be allowable if rewritten into independent form to include all the limitations of the base claim and intervening claims. Applicants have canceled these claims but have included their substantive features in new claims 16-22. Particularly, substantive features of claim 3 have been presented as new independent claim 16, substantive features of claim 5 have been presented as new independent claim 18, the substantive features of claim 13 have been presented as independent claim 21, and the substantive features of claim 15 have been presented as new independent claim 22. Although the new claims are not verbatim of the canceled claims, applicants respectfully submit that the changes, e.g., adding articles, changing plural tense to singular tense and replacing "characterised" by with "comprising" are made to conform the claims to typical U.S. prosecution practice and do not narrow their scope. Also, new claims 18, 21, and 22 are defined as including both tetrahydrofolic acid and tetrahydrofolic acid ester.

Claims Rejections Under 35 U.S.C. § 112, 2nd Paragraph and Other Claim Amendments

Applicants have amended claims 11, 12 and 14 to obviate these rejections. Applicants respectfully submit that inserting an article before "boiling temperature," correcting the spelling of the term "mixtures," and deleting the terminology "under esterifying conditions" from claim 14, do not narrow the scope of these claims. In addition, the claims 1, 2, 6, 7, 10-12, and 14, have been amended to replace "characterised in that"

with --wherein-- or replacing "characterised by" with --comprising--. In addition, some words have been replaced with their American English counterparts, e.g., "hydrolysing" with --hydrolyzing--. Applicants respectfully submit that these changes do not narrow the scope of the claims, and respectfully submit that these rejections be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

Claims 1-2, 6, 7, and 10-12 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,324,836 (Müller). Applicants respectfully traverse these rejections as applicable to the present claims.

Müller discloses and claims a process for the fractionated crystallization of tetrahydrofolic acid, sulphonic acid and sulphuric acid addition salts out of a solvent containing water.

However, Müller fails to teach or suggest fractionated crystallization of a tetrahydrofolic acid ester addition salt with aromatic sulfonic acids in organic salt. Consequently, Müller cannot anticipate the claimed invention. Moreover, applicants have amended claim 2 to exclude a tetrahydrofolic acid to clarify that the tetrahydrofolic acid esters as defined in claim 1 do not include a tetrahydrofolic acid. Additionally, Müller is discussed in the present specification at page 3, lines 1-9. Particularly:

The process described in EP-0 495 204 uses the equimolar mixtures of (6S,αS) and (6R,αS) diastereomers of tetrahydrofolic acid sulphonic acid salts, which are dissolved in water and then crystallized. This process results in concentration of the desired (6S,αS) diastereomers, it being possible to already achieve very high concentrations in the first crystallisation step (up to about 95%) and to obtain pure (6R,αS) tetrahydrofolic acid by a further fractionated crystallisation. This process is not a serious contender, *inter alia* from the economic viewpoint, since the sulphonic acids used for the salt formation can only be isolated from aqueous mother liquors with great effort, and it therefore becomes necessary to dispose of large volumes of mother liquors containing sulphonic acid, which is uneconomical.

In addition, the present invention provides significant and unexpected results not appreciated by Müller. Particularly, the present invention exemplifies a much higher depletion factor than that exemplified by Müller. A depletion factor can be calculated by subtracting the starting material percent from a 100%, and dividing that difference by the difference of a 100% minus the final product purity. A comparison of these examples are depicted below. Examples B1a-1d and B2 are disclosed in the present application at pages 15-18.

Present Application

EXAMPLE	SALT PARTNER	OPTICAL PURITY		DEPLETION FACTOR
		STARTING MATERIAL	PRODUCT	
B1b	Benzene sulphonic acid	34.0%	96.6%	19
B1a	Benzene sulphonic acid	74.0%	99.0%	26
B1c	Benzene sulphonic acid	50.0%	99.1%	56
B1d	Benzene sulphonic acid	70.0%	99.9%	300
B2	Toluene sulphonic acid	50.0%	99.1%	56

Müller

EXAMPLE	SALT PARTNER	OPTICAL PURITY		DEPLETION FACTOR
		STARTING MATERIAL	PRODUCT	
7b	Benzene sulphonic acid/hydrochloric acid	50.0%	91.6%	6
7a	Benzene sulphonic acid	50.0%	92.4%	7
10	Benzene sulphonic acid	50.0%	94.2%	9
1	Toluene sulphonic acid	50.0%	86.7%	4
5	Toluene sulphonic acid	50.0%	91.4%	6
6	Toluene sulphonic acid	50.0%	91.5%	6
3	Toluene sulphonic acid	50.0%	92.5%	7
2	Toluene sulphonic acid	50.0%	93.6%	8
4	Toluene sulphonic acid	50.0%	94.7%	9
9	Toluene sulphonic acid	50.0%	95.4%	11

Consequently, the present invention as exemplified above provides a much greater depletion factor not obtained nor appreciated by Müller. Consequently, applicants respectfully submit that the prior art rejections should be withdrawn.

Information Disclosure Statement

Attached is an Information Disclosure Statement citing the EP applications cited in the search reports. Also cited are published US applications and patents corresponding as stated in the Information Disclosure Statement.

In view of the above, favorable reconsideration is courteously requested. If there are any remaining issues which can be expedited by a telephone conference, the examiner is courteously invited to telephone counsel at the number indicated below.

In addition, applicants respectfully submit that the examiner should acknowledge that copies of the certified copies of the priority documents have been received in this national stage application from International Bureau from the next paper from the Office.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

James E. Ruland, Reg. No. 37,432
Attorney for Applicants

MILLEN, WHITE, ZELANO &
BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: EPROV-18

Date: October 15, 2003

K:\eprov\18\Reply to 7-15-03 OA.doc